UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION	**MDL No. 2875**
THIS DOCUMENT RELATES TO ALL CASES	**HON. ROBERT B. KUGLER** **CIVIL NO. 19-2875 (RBK)**

PLAINTIFFS' BRIEF IN SUPPORT OF *DAUBERT* MOTION TO PRECLUDE OPINIONS OF DEFENSE EXPERT AKHILESH NAGAICH, PH.D.

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PRELIMINARY STATEMENT

This motion arises against the backdrop of the disturbing news that generic manufacturing processes designed to cut costs had allowed NDMA and NDEA to be formed while manufacturing valsartan. Previously this Court stated: "The Valsartan MDL arose from an extensive Food and Drug Administration ["FDA"] recall in the U.S. of generic hypertensive, prescription drugs ["Valsartan" or "Valsartan-containing drugs" or "VCD'S"]. To be clear, as used herein, the term "VCD" refers to valsartan-containing drugs that were contaminated with probable genotoxic human carcinogens in the form of nitrosamines, N-nitrosodimethylamine ("NDMA") and N- N-nitrosodiethylamine ("NDEA")." ECF 2261 at 2. Furthermore, this Court previously recognized that: "It is further incontrovertible in the morass of factual and legal arguments here that the contamination resulted from defendants' non-compliance of cGMPs at some level." *Id* at 21.

Akhilesh Nagaich, Ph.D., claims to be a consultant for cGMPs with a background in chemistry. [redacted]

genotoxins, but admitted that he never reviewed any of these testing for ZHP or the support given to Torrent for these statements.

[redacted]

STATEMENT OF FACTS

On page 8 of his expert report, Dr. Nagaich boils down his opinions into four categories – 1) "that Torrent met all regulatory obligations for sourcing Valsartan API and conducted adequate independent testing of incoming API lots", 2) that "Torrent also met its regulatory obligations with regard to patient safety by promptly and voluntarily issuing recalls", 3) "that Torrent used a robust supplier qualification program to conduct risk assessments for its Valsartan API supplier, Zhejiang Huahui Pharmaceutical Co. Ltd." (hereinafter referred to as "ZHP"), and 4) an overarching opinion "that Torrent fully complied with cGMP regulations".[1] [redacted]

[1] Ex 1 (Nagaich 12/22/22 Rpt.) at 8.

[redacted] At deposition, Dr. Nagaich revealed that he did not consider whether the chemistry used to produce ZHP's valsartan API would have been foreseeable to Torrent for the possibility of NDMA formation. [redacted] Without knowing whether or not Torrent should be on alert for certain chemical formations, Dr. Nagaich could not opine as to whether Torrent conducted adequate testing for the chemicals that they should have been on alert that could form in ZHP's valsartan API.

[2] Ex. 2 (Nagaich 2/9/22 Depo. Tr.) at 40:15-20.
[3] Ex. 2 at 39-48.
[4] Ex. 2 at 196:4-17.
[5] Ex. 2 at 206:7-209:5.
[6] Ex. 2 at 210:2-216:18.
[7] Ex. 2 at 217:18-224:1.

Next, Dr. Nagaich opined in his expert report that Torrent acted swiftly and responsibly in initiating a recall.[8] [redacted]

[8] Ex. 1 at 8.

[9] Ex. 3 (TORRENT-MDL2875-00072542) – Dawn Chitty in email states: "FDA is expecting that we are going to prove that there is no NDMA in the API batches that we have used. They are not going to let us release any product until there is conclusive proof. The statements from the vendor are not sufficient. I'm not sure what we need to do but there has to be some method for evaluating this impurity and we need to get it verified/validated as soon as possible."

[10] Ex. 2 at 106:14-21.

[11] Ex. 2 at 109:22-110:3, 111:18-24, and 114:11-23.

[12] Ex. 2 at 127:4-130:22.

[13] Ex. 2 at 144:11-145:9.

[14] Ex. 2 at 145:11-148:6. See also Ex. 9 (FDA Inspection Report of ZHP Facility) at page 8 where FDA Inspector Clausen writes: "On August 1, 2018, I asked Mr. Du if the firm tested Valsartan API manufactured for the Chinese market using Process II (TEA) manufacturing

Dr. Nagaich completely ignored all of the documents and issues which run contrary to his opinion that Torrent acted promptly in initiating a recall of its valsartan products.

Finally, Dr. Nagaich opined in his expert report that Torrent fully complied with cGMP guidelines.[15] [redacted] In deposition, Dr. Nagaich was then shown a document that he failed to consider and was pivotal to his opinion. Specifically, Dr. Nagaich was

process for NDMA and if so, the results of those tests. On August 2, 2018, Mr. Du stated the firm tested Valsartan API manufactured for the Chinese market using Process I] (TEA) manufacturing process and found from 11 ppm to 107 ppm NDMA in the batches tested."

[15] Ex. 1 at 8.
[16] Ex. 2 at 301:13-302:9.
[17] Ex. 2 at 221:5-222:9.
[18] *Id*.
[19] See Ex. 4 (Baertschi 1/26/23 Depo. Tr.) at 264, wherein Teva's defense expert, Dr. Baertschi, admitted that the USP monograph for valsartan is based on Diovan's name-brand TIN (tributyltin) process that did not contain sodium nitrite.
[20] Ex. 2 at 224:3-228:2.
[21] Ex. 2 at 313:10-315:5.

shown USP General Notices and Requirements chapter 5.60 which discusses that additional testing, (other than just the specifications in the monograph), shall be done when there is a change in the manufacturing process.[22] [redacted] As a result of Dr. Nagaich's failure to consider the most relevant documents as to the appropriate guidelines for cGMP's, Dr. Nagaich's opinions should be excluded.

THE *DAUBERT* STANDARD

Federal Rules of Evidence 702 provides the standard for admissibility of expert testimony. "As a gatekeeper, courts are supposed to ensure that the testimony given to the jury is reliable and will be more informative than confusing." *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 858 F.3d 787, 800 (3d Cir. 2017). Additionally, "[b]oth an expert's methodology and the

[22] Ex. 5 (USP General Notices and Requirements) at 4 states: "Nonmonograph tests and acceptance criteria suitable for detecting and controlling impurities that may result from a change in the processing methods or that may be introduced from external sources should be employed in addition to the tests provided in the individual monograph, where the presence of the impurity is inconsistent with applicable good manufacturing practices or good pharmaceutical practices."
[23] Ex. 2 at 324:7-326:23.

application of that methodology must be reviewed for reliability." *Id.* at 791. The "specific way an expert conducts such an analysis must be reliable; '**all of the relevant evidence must be gathered**, and **the assessment or weighing of that evidence must not be arbitrary**, but must itself be **based on methods of science.**'" *Id.* at 796.

The party offering the proposed expert testimony bears the burden of establishing the admissibility of the testimony by a preponderance of the evidence. *Padillas v. Stork-Gamco, Inc.,* 186 F.3d 412, 417-18 (3d Cir. 1999). An "expert's opinions must be based on the methods and procedures of science, rather than on subjective belief or unsupported speculation." *In re Paoli R.R. Yard PCB Litigation, 35 F.3d 717, 742 (3d Cir. 1994)* (citations and internal quotations omitted). Thus, "the expert must have 'good grounds' for his or her belief." *Id.* (quoting *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 590 (1993)).

Furthermore, "*Daubert*'s gatekeeping requirement .... make[s] certain that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.'" *Elcock v. Kmart Corp.*, 233 F.3d 734, 746 (3d Cir. 2000) (quoting *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999)); *see also Magistrini v. One Hour Martinizing Dry Cleaning*, 180 F. Supp. 2d 584, 594 (D.N.J. 2002*), aff'd,* 68 Fed. Appx. 356 (3d Cir. 2003). In addition, the following factors are relevant when determining reliability:

> (i) whether the expert's proposed testimony grows naturally and directly out of research the expert has conducted independent of the litigation; (ii) whether the expert has unjustifiably extrapolated from an accepted premise to an unfounded conclusion; (iii) whether the expert has adequately accounted for alternative explanations.

Magistrini, 180 F. Supp. 2d at 594–95, internal citations omitted. To this end, the Third Circuit has affirmed the exclusion of expert testimony that "failed to consistently apply the scientific

methods … articulate[d], … deviated from or downplayed certain well-established principles of [the] field, and … inconsistently applied methods and standards to the data so as to support [an] a priori opinion." *Zoloft*, 858 F.3d at 792. In addition, this Court excluded an expert in part because the expert failed to satisfy the reliability requirement, as the expert failed to consider important facts without satisfactory explanation, among other things. *Player v. Motiva Enterprises LLC*, No. Civ. 02–3216(RBK), 2006 WL 166452, at *7 (D.N.J. Jan. 20, 2006).

ARGUMENT

I. DR. NAGAICH'S OPINION THAT TORRENT DID NOT VIOLATE ANY cGMP GUIDELINES BECAUSE TORRENT MANUFACTURED VALSARTAN IN ACCORDANCE WITH THE VALSARTAN MONOGRAP SPECIFICATIONS SHOULD BE EXCLUDED, BECAUSE DR. NAGAICH FAILED TO CONSIDER WHETHER TORRENT FOLLOWED SECTION 5.6 OF THE GENERAL CHAPTERS OF USP

[redacted] In other words, since the USP monograph for valsartan allows impurities at a level below .1% and since the amount of NDMA in each pill was below .1%, Dr. Nagaich opined that Torrent followed all quality expectations, and therefore, followed the cGMP guidelines.[25] However, as to quality expectations, Dr. Nagaich failed to recognize the applicable USP General Notices and Requirements. USP General Notices and Requirements chapter 5.60 declares that additional testing, (other than just the specifications in the monograph), shall be done when there is a change in the manufacturing process.[26] [redacted]

[24] Ex. 2 at 221:5-222:9.
[25] Ex. 6 (Valsartan USP Monograph Jan. 28, 2022).
[26] Ex. 5 (USP General Notices and Requirements) at 4 states: "Nonmonograph tests and acceptance criteria suitable for detecting and controlling impurities that may result from a change in the processing methods or that may be introduced from external sources should be employed in addition to the tests provided in the individual monograph, where the presence of the impurity is inconsistent with applicable good manufacturing practices or good pharmaceutical practices."

[redacted] Dr. Nagaich had obviously not reviewed the requisite documents to reach

[27] See Ex. 4 (Baertschi 1/26/23 Depo. Tr.) at 264, wherein Teva's defense expert, Dr. Baertschi, admitted that the USP monograph for valsartan is based on Diovan's name-brand TIN (tributyltin) process that did not contain sodium nitrite.
[28] Ex. 2 at 227:10-20.
[29] Ex. 2 at 308:10-311:14.
[30] Ex. 2 at 310:6-311:14.
[31] Ex. 2 at 313:10-315:5.
[32] Ex. 2 at 324:7-326:23.

an informed expert opinion, and therefore, his opinions regarding Torrent not having any cGMP violations should be excluded.

II. DR. NAGAICH'S OPINION THAT TORRENT MET ITS REGULATORY OBLIGATIONS BY SWIFTLY ISSUING RECALLS SHOULD BE EXCLUDED, BECAUSE DR. NAGAICH FAILED TO INVESTIGATE OR CONSIDER ANY OF THE DOCUMENTS AND ISSUES RELATED TO WHETHER TORRENT COULD HAVE DISCOVERED NDMA IN ITS PRODUCTS SOONER

Dr. Nagaich also opined in his expert report that Torrent met its regulatory obligations by swiftly issuing recalls once it became aware that its products had NDMA and NDEA in them.[33]

[redacted] Dr.

[33] Ex. 1 at 8.
[34] Ex. 2 at 79:6-21.
[35] Ex. 7 (TORRENT-MDL2875-00131251).
[36] Ex. 8 (PRINSTON00304075).
[37] Ex. 3 (TORRENT-MDL2875-00072542).
[38] Ex. 10 (TORRENT-MDL2875-00516411) at 3.
[39] *Id*. at 2.

[redacted]

[40] Ex. 2 at 70:4-72:18 and 80:16-84:11.
[41] Ex. 2 at 82:16-89:17.
[42] Ex. 3.
[43] Ex. 3 Arunesh Verma states: "All customers have been back-ordered and every single day counts, as our failure to supply penalties will start kicking in…" and Ex. 11 (TORRENT-MDL2875-00007067) Arunesh Verma asks: "What is annual budget sales & margin impact if we were to discontinue all Valsartan containing products?"
[44] Ex. 2 at 106:14-21.
[45] Ex. 2 at 109:22-110:3, 111:18-24, and 114:11-23.

[redacted] Dr. Nagaich failed to consider how long it would have taken Torrent to develop an in-house testing method for NDMA, he failed to consider whether Torrent ever attempt to contract a lab to test for NDMA and he failed to consider whether Torrent could have simply requested ZHP to test old process valsartan for NDMA. Without considering any of these issues, Dr. Nagaich simply cannot give an informed opinion as to whether Torrent met its regulatory obligations by swiftly recalling valsartan, and therefore, these opinions should be excluded.

III. DR. NAGAICH'S OPINION THAT TORRENT CONDUCTED ADEQUATE TSTING OF THE INCOMING VALSARTAN API SHOULD BE EXCLUDED, BECAUSE DR. NAGAICH FAILED TO INVESTIGATE OR CONSIDER ANY OF THE DOCUMENTS RELATED TO WHETHER TORRENT SHOULD HAVE BEEN ON HEIGHTENED ALERT OF POTENTIAL NDMA AND

[46] Ex. 2 at 127:4-130:22.
[47] *Id*.
[48] Ex. 2 at 144:11-145:9.
[49] Ex. 2 at 145:11-148:6. See also Ex. 9 (FDA Inspection Report of ZHP Facility) at page 8 where FDA Inspector Clausen writes: "On August 1, 2018, I asked Mr. Du if the firm tested Valsartan API manufactured for the Chinese market using Process II (TEA) manufacturing process for NDMA and if so, the results of those tests. On August 2, 2018, Mr. Du stated the firm tested Valsartan API manufactured for the Chinese market using Process I] (TEA) manufacturing process and found from 11 ppm to 107 ppm NDMA in the batches tested."

NDEA FORMATION, AND THEREFORE, TESTED THE VALSARTAN API TO ENSURE IT DID NOT CONTAIN NDMA OR NDEA

Finally, Dr. Nagaich gave the expert opinion that Torrent conducted adequate testing of the incoming API.[50] In reaching this opinion, Dr. Nagaich ignored the information that demonstrated the relevant type of testing that Torrent should have conducted. In order to understand the requisite testing that Torrent should have conducted, Dr. Nagaich needed to consider what potential impurities may be in the valsartan that it manufactured. [redacted] Without doing the research to understand the historical scientific knowledge of what chemicals could be combined in medications to form NDMA and/or without understanding what knowledge Torrent had in terms of what chemicals are being combined to manufacture ZHP's old process valsartan API, Dr. Nagaich would not be able to give an informed opinion as to whether Torrent had knowledge that it should be testing for potential NDMA formation. As a result, Dr. Nagaich's opinion ignores the key documents required to reach an informed expert opinion on whether Torrent conducted adequate testing, and therefore, this opinion should be excluded.

[50] Ex. 1 at 8.
[51] Ex. 2 at 196:4-17.
[52] Ex. 2 at 206:7-209:5.
[53] Ex. 2 at 210:2-216:18.

CONCLUSION

For the foregoing reasons, Akhilesh Nagaich, Ph.D. should be precluded from offering his opinions related to liability in this case.

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that on March 13, 2023 , a true and correct redacted copy of the foregoing was filed and served via the court's CM/ECF system, and an unredacted version was served on the court and the Defense Executive Committee via email.

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